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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/937,946	10/07/2002	Richard J Roman	650053--.91533	8704

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EXAMINER
SWOPE, SHERIDAN

ART UNIT	PAPER NUMBER
1656	

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DATE MAILED: 04/05/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/937,946	ROMAN ET AL.	
	Examiner	Art Unit	
	Sheridan L. Swope	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 January 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,7-11,15,17 and 37-44* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,7-11,15,17 and 37-44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response of January 10, 2006 to the First Action on the Merits mailed July 14, 2005 is acknowledged. It is acknowledged that Applicants have cancelled Claims 2-6, 12-14, 16, and 18-36, amended Claims 1, 7-11, and 15, and added Claims 37-44. Claims 1, 7-11, 15, 17, and 37-44 are pending and are hereby examined.

Specification-Objections

Objection to the title for not being descriptive of the elected invention, a method of treatment using HET-0016, is maintained.

Claims-Objections

Objection to the claim set for not beginning with a sentence of which the claims are an object is maintained.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Double Patenting

Rejection of Claims 1, 7-11, 15, and 17 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claims 1-4, 6-13, 19-22, and 24-28 of US Application No. 10/986,695 is maintained. Claims 37-44 are herein also rejected under 35 U.S.C. 101, double patenting, as being unpatentable over Claims 1-4, 6-13, 19-22, and 24-28 of US Application No. 10/986,695. Applicants' state in their response that they "stand ready to address the rejection should it be maintained as an actual rejection.

Claim Rejections - 35 USC § 112-First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Enablement

Rejection of Claims 1, 7-11, 15, and 17 under 35 U.S.C. 112, first paragraph lack of enablement, is maintained. Claims 37-44 are herein rejected for the same reasons. As described in the prior action the specification does not reasonably provide enablement for all methods of treating cerebral vascular disease using any compound that decreases the activity of any CYP4A or CYP4F 20-HETE synthesizing enzyme. The specification fails to support the full scope of Claims 1, 7-11, 15, 17, and 37-44 because it fails to teach (A) the structure of all 20-HETE synthesizing enzymes that are of the CYP4A or CYP4F subclass; (B) the structure of all compounds that are inhibitors of any said CYP4A or CYP4F enzymes; (C) how any said compound can and cannot be modified and still inhibit any CYP4A or CYP4F enzyme; (D) the structure of inhibitors of any CYP4A or CYP4F enzyme that can be successfully used for treatment of the recited cerebral vascular diseases; (E) how any said inhibitor can and cannot be modified and still be successfully used for treatment of the recited cerebral vascular diseases; (F) a rational and predictable scheme for modifying any compound, formulation, or administration route with an expectation of obtaining the desired treatment result; (G) the target population to be treated (see Hoagland et al, 2003); and (H) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

In support of their request that said rejection be withdrawn, Applicants provide the following arguments.

(A) Identifying new 20-HETE synthesizing enzyme inhibitors, either by testing new compounds or modifying existing inhibitors, is not part of the invention. The present invention only calls for the use of known inhibitors and those that will be come known. The application provides examples of 20-HETE synthesizing enzyme inhibitor e.g. HET0016, 17-ODYA, DDMS, ABT, and miconazole. The skilled artisan will certainly become familiar with any new inhibitors. When an enzyme and inhibitors are well known, a single example is sufficient for the specification to be adequate.

(B) The enablement is not applicable to future technologies (Chiron Corp v Genetech Inc, 363 F.3d 1247 (Fed Cir. 2004).

(C) The PTO considers a claim reciting the use of any inhibitor to an enzyme patentable if a few examples are provided in the specification.

These arguments are not found to be persuasive for the following reasons.

(A) Reply: For the full scope of the recited invention to be practiced, either the specification or the prior art, at the time of filing, must enable the recited invention MPEP 2164.05(a) [R-2]. Neither the specification nor the prior art enable the skilled artisan to make and use the full scope of treating the recited cerebral vascular diseases with any inhibitor of any CYP4A or any CYP4F enzyme, wherein in the inhibitor has any structure and, wherein the enzyme has any structure. It is acknowledged that the specification teaches that HET0016 is an inhibitor of CYP4A11 and CYP4F2 (Fig 11). It is also acknowledged that the art teaches that DDMS is an inhibitor of HETE synthesis by CYP4A1 and CYP4A3 enzymes (Wang et al, 1998;

pg 971, parg 2). However, neither 17-ODYA nor miconazole are specific inhibitors of CYP4A or CYP4F and DDMS has not been shown to inhibit CYP4F. In addition, PPOH inhibits CYP4A3 but not CYP4A1. Thus, only a single example of an inhibitor of CYP4F has been disclosed; therefore, the skilled artisan is not in possession of sufficient guidance to make and use any inhibitor of CYP4F. Furthermore, HET0016 has been shown to inhibit only a single member of each of the CYP4A subtype of HETE synthesizing enzymes, CYP4A11. DDMS is the only compound that has been shown to inhibit more that a single member of the CYP4A subfamily. Based on such teachings, neither the prior art or the specification provide sufficient guidance to enable the skilled artisan to make and use a method of treatment using any inhibitor of any CYP4A enzyme, wherein in the inhibitor has any structure and, wherein the CYP4A has any structure.

(B) Reply: As stated in MPEP 2164.05(a) [R-2], the specification must be enabling as of the filing date of the application. MPEP 2164.03(a) [R-2] states that, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification needs more detail as to how to make and use the invention in order to be enabling. In Chiron Corp. v. Genentech Inc., 363 F.3d 1247, 1254, 70 USPQ2d 1321, 1326 (Fed. Cir. 2004) is was stated that: "Nascent technology must be enabled with a specific and useful teaching. The law requires an enabling disclosure for nascent technology because a person of ordinary skill in the art has little or no knowledge independent from the patentee's instruction. Thus, the public's end of the bargain struck by the patent system is a full enabling disclosure of the claimed technology." The reasons the full scope of elected invention is not enabled are described above and in the prior action.

(C) Reply: Claim 1 does not recite an inhibitor to a specific enzyme of known structure and function. Claim 1 recites any inhibitor of any enzyme that has the activity of any member of the CYP4A or CYP4F subfamilies of HETE synthesizing enzymes, wherein the enzyme has any structure. As described in (A), above, the specification teaches the structure of only a single inhibitor of a single member of all CYP4F enzymes. As also described above, the specification teaches the structure of only a single inhibitor of a single member of all CYP4A enzymes and the prior art teaches the structure of a single inhibitor of two different members of the CYP4A subfamily. Said examples to not provide sufficient guidance such that one of skill in the art would not know how to make compounds that inhibit any CYP4A or CYP4F enzyme, as recited in the instant invention.

Written Description

Rejection of Claims 1, 7-11, 15, and 17 under 35 U.S.C. 112, first paragraph, written description, is maintained. Claims 37-44 are herein rejected for the same reasons. As described in the prior action, said claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The specification does not reasonably described the genus of all methods of treating the recited cerebral vascular diseases using any compound that decreases the activity of any CYP4A or CYP4F 20-HETE synthesizing enzyme.

In support of their request that said rejection be withdrawn, Applicants provide the following arguments. The application clearly conveys that CYP4A and CYP4F inhibitors can be used to treat the four specific cerebral vascular diseases recited in amended Claim 1.

This argument is not found to be persuasive for the following reasons. It is acknowledged that the specification teaches the compound HET0016, which is an inhibitor of CYP4A11 and CYP4F2 and is, more likely than not, useful for treating the recited vascular diseases. However, the specification fails to describe the full scope of the genus of methods for treatment using any compound that decreases the activity of any enzyme, with any structure, having the function of a CYP4A or CYP4F 20-HETE synthesizing enzyme. The specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Rejection of Claims 1 and 17 under 35 U.S.C. 102(a) as being anticipated by Alonso-Galicia et al, 1999, is maintained, as evidenced by Wang et al, 1998 (IDS). Claims 37, 39, and 41 are herein rejected under 35 U.S.C. 102(a) as also being anticipated by Alonso-Galicia et al, 1999. As previously described, Alonso-Galicia et al teach that intracerebroventricular injection of DDMS reduces cerebral blood flow (Fig 7). As evidenced by Wang et al, DDMS inhibits CYP4A1 and CYP4A3 (pg 971, parg 2). Claims 37, 39, and 41, as dependent from Claim 1 and further reciting treatment of stroke, administered into the cerebrospinal fluid, and treatment of rat, respectively, are also rejected under 35 U.S.C. 102(a) as being anticipated by Alonso-Galicia

et al, 1999. Therefore, Claims 1, 17, 37, 39, and 41 are rejected under 35 U.S.C. 102(a) as being anticipated by Alonso-Galicia et al, 1999, as evidenced by Wang et al, 1998.

Rejection of Claim 1 under 35 U.S.C. 102(b) as being anticipated by Su et al, 1999, as evidenced by Fotherby et al, 1997 or Schmidt et al, 2000, is maintained. Claims 37, 39, and 41 are herein rejected under 35 U.S.C. 102(a) as also being anticipated by Su et al, as evidenced by Fotherby et al or Schmidt et al. As previously described, Su et al teach that 1-ABT reduces the synthesis of 20-HETE (Fig 1) and reduces blood pressure in rat (Fig 9), which, as is well known in the art, is an effective means to treat cerebral vascular diseases (Fotherby et al or Schmidt et al). As further taught by Su et al, 1-ABT decreases expression of the HETE synthesizing enzyme CYP4A1. Claims 37 and 41, as dependent from Claim 1 and further reciting treatment of stroke and treatment of rat, respectively, are also rejected under 35 U.S.C. 102(b) for the same reasons. Therefore, Claims 1, 37, and 41 are rejected under 35 U.S.C. 102(b) as being anticipated by Su et al, 1999, as evidenced by Fotherby et al, 1997 or Schmidt et al, 2000.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Rejection of Claim 1 under 35 U.S.C. 103(a) as being unpatentable over Roman et al, 1999 in view of Frisbee et al, 2000, is maintained. Claims 15, 37, and 39-41 are here rejected under 35 U.S.C. 103(a) as also being unpatentable over Roman et al, 1999 in view of Frisbee et al, 2000. As set forth in the prior action, Roman et al teach that cerebral vascular diseases,

including cerebral vasospasm, stroke, and hypertension, and migraine, can be treated by blocking the effects of 20-HETE (pg 5, lines 1-4), while Frisbee et al teach that treatment of rats with 17-ODYA or DDMS inhibits 20-HETE production (pg H1518, parg 4-5) and thereby reduces vascular vessel diameter (Figs 2, 4, 6, and 8). As also taught by Frisbee et al, 17-ODYA and DDMS inhibit P450 ω-hydroxylase, a 20-HETE synthesizing enzyme of the CYP4A subclass. For the reasons explained in the prior action, the skilled artisan would be motivated to combine Roman et and Frisbee et al, to use 17-ODYA or DDMS to treat stroke. Claims 15 and 39, 37, and 40, as dependent from Claim 1 and further reciting intravenous administration, treatment of stroke, and treatment of humans, as taught by Roman et al (pg 62, parg 3; pg 5, parg 1; pg 11, parg 6, respectively) are also rejected under 35 U.S.C. 103(a) for the same reasons. Claim 41, as dependent from Claim 1 and further reciting treatment of rat, as taught by Frisbee et al (pg H1518, parg 4-5) is also rejected under 35 U.S.C. 103(a) for the same reasons. Therefore, Claims 1, 15, 37, and 39-41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Roman et al, 1999 in view of Frisbee et al, 2000.

Claims 1, 15, and 37-43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Roman et al, 1999 in view of Powell et al, 1998 (IDS) or Lasker et al, 2000. Roman et al teach that cerebral vascular diseases, including cerebral vasospasm and stroke, can be treated by blocking the effects of 20-HETE (pg 5, lines 1-4). Roman et al do not teach treatment of cerebral vascular diseases with an inhibitor of 20-HETE synthesis. Both Powell et al (Fig 4) and Lasker et al (Fig 4 & 5) teach that the HETE synthesis by CYP4A11 and CYP4F2 can be inhibited by an antibody to the respective enzyme. It would have been obvious to a person of ordinary skill in the art to administer the antibodies of Powell et al or Lasker et al intravenously

for treatment of cerebral vascular disease. Motivation to do so is provided by Powell et al (pg 1335, parg 1) and Lasker et al (pg 4125, parg 4), wherein they state that elevated 20-HETE levels, via CYP4A11 and/or CYP4F2 contributes to hypertension and vasocontriction, which are well known in the art to be causative factors and/or exacerbate cerebral vascular disease. The expectation of success is high, as the antibodies taught by Powell et al and Lasker et al are known inhibitors of 20-HETE synthesis. Therefore, Claims 1, 15, and 37-43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Roman et al, 1999 in view of Powell et al, 1998 (IDS) or Lasker et al, 2000.

Applicant's amendment necessitated any new grounds of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Regarding filing an Appeal, Applicants are referred to the Official Gazette Notice published July 12, 2005 describing the Pre-Appeal Brief Review Program.

To insure that each document is properly filed in the electronic file wrapper, it is requested that each of amendments to the specification, amendments to the claims, Applicants' remarks, requests for extension of time, and any other distinct papers be submitted on separate pages. It is also requested that Applicants identify support, within the original application, for any amendments to the claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheridan L. Swope whose telephone number is 571-272-0943. The examiner can normally be reached on M-F; 9:30-7 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr can be reached on 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published application may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on the access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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PRIMARY EXAMINER